

Refer to: Ganz PA, Vernon SE, Preston D, et al: Lung cancer in younger patients. West J Med 133:373-378, Nov 1980

Lung Cancer in Younger Patients

PATRICIA A. GANZ, MD, *Sepulveda, California*; STEPHEN E. VERNON, MD;
DALE PRESTON, PhD, and WALTER F. COULSON, MD, *Los Angeles*

Carcinoma of the lung is rare in younger patients, but occasional reports of this condition have appeared in the literature. This article reviews the clinical and pathological patterns of bronchogenic carcinoma in 96 patients, 40 years old or younger seen at UCLA (University of California, Los Angeles) Hospital between 1956 and 1976. This review confirms the finding in other reports of a higher proportion of women among younger patients with lung cancer as well as a relatively low incidence of squamous cell carcinoma. Using comparative data from the UCLA and California tumor registries, we could find no significant difference in survival of the younger patients when compared with the general population of patients with lung cancer.

CARCINOMA OF THE LUNG occurs most commonly in men in the sixth and seventh decades of life.¹ In our patient population we are also seeing younger patients; many of them are women. Occasional reports of lung cancer in young patients have appeared in the literature.²⁻⁹ Some of these have emphasized the appearance of tumors in the very young,³ but more often they have dealt with populations younger than 40 or 45 years of age. Several of these reports consider only male patients, and relevant smoking or occupational history has not been included.

The present study was undertaken to review

the experience at the UCLA (University of California, Los Angeles) Hospital with bronchogenic carcinoma occurring in male and female patients 40 years of age and younger between 1956 and 1976. We examined clinical presentation, smoking and occupational history, tumor histology and survival in these patients.

Patients and Methods

The UCLA Hospital is a university teaching hospital that was opened in 1956, and serves the greater Los Angeles area as a referral center for difficult diagnostic or therapeutic medical problems. The patient population seen at this hospital has been largely white and middle-class, but medically indigent patients and private patients of local practitioners are also cared for.

The hospital tumor registry routinely reviews and abstracts the records of all patients seen at UCLA with a diagnosis of a malignant tumor. Basic data on each patient (such as age, sex, tumor type) have been stored on computer tape and registry data on specific tumors can be retrieved.

A list of all patients 40 years of age and

From the Division of Hematology/Oncology, Department of Internal Medicine, UCLA School of Medicine, San Fernando Valley Program, Sepulveda (Dr. Ganz); the Department of Pathology (Dr. Vernon), UCLA Cancer Center Base Unit (Dr. Preston) and the Division of Surgical Pathology (Dr. Coulson), UCLA School of Medicine.

Dr. Vernon is a regular Clinical Fellow of the American Cancer Society (CF#4281).

This study was supported in part by a grant from the Brown and Williamson Tobacco Corp.; Phillip Morris Incorporated; R. J. Reynolds Tobacco Co.; the United States Tobacco Company, and the Tobacco Associates, Inc. Computing assistance was obtained from the Health Sciences Computing Facility, UCLA, supported by NIH Special Research Resources Grant RR-3.

Submitted, revised, February 4, 1980

Reprint requests to: Patricia A. Ganz, MD, Division of Hematology/Oncology (111B), Dept. of Medicine, Veterans Administration Medical Center, 16111 Plummer St., Sepulveda, CA 91343.

LUNG CANCER IN YOUNGER PATIENTS

younger with lung cancer seen at UCLA Hospital between January 1, 1956, and December 31, 1976, was obtained using the Tumor Registry computer file. For the purpose of this report only those cases of bronchogenic carcinoma were included. Nine patients with carcinoid tumors and one with a primary sarcoma were excluded.

Ninety-six patients 40 years of age and younger with bronchogenic carcinoma had been seen during the stated period. Hospital charts, radiotherapy records and tumor registry abstract files were reviewed to obtain the following information: age at diagnosis, sex, race, date of diagnosis, date of death, stage and Karnofsky performance status at diagnosis, smoking and occupational history, and search for another primary source in case of adenocarcinoma.

An attempt was made to review the diagnostic histologic specimen of each patient. Cytologic specimens were not used. Many patients had been referred to UCLA after a diagnostic biopsy was done at their local hospital; some, but not all of these specimens could be obtained for reexamination. We were able to review 61 of the 96 original specimens (64 percent). Autopsy material was reviewed in 23 cases but in 7 of these the original biopsy specimen was not available; therefore, 68 of 96 cases (71 percent) had the pathological diagnosis reviewed.

The specimens were examined by the pathologists without benefit of clinical information. When tissue blocks were available, new sections were cut and appropriate special stains were obtained. A modification of the World Health Organization (WHO) system was used in classifying the lesions. When tissue specimens were not available for reexamination, the pathological diagnosis as initially reviewed by our pathology department was recorded.

Additional comparative data from the entire UCLA Tumor Registry patient population with lung cancer and from the California State Tumor Registry will be used as a basis for comparison.

Clinical and Pathological Findings

Age, Sex and Racial Distribution

In our study group the youngest patient was 25 years old and the oldest was 40 at diagnosis. The median age was 37 years, with the diagnosis made in 40 percent of the patients at age 39 or 40. There was no significant difference in age distribution between the two sexes. In the youngest patient squamous cell carcinoma developed in a

TABLE 1.—*Age and Sex Distribution of Patients*

Age	No. of Men		No. of Women		Total No. of Patients	
	Percent	Percent	Percent	Percent	Percent	Percent
25-29 ...	0	0	1	3	1	1
30-34 ...	15	25	7	20	22	24
35-39 ...	34	56	20	57	54	55
40	12	19	7	20	19	20
TOTAL	61		35		96	100

previously irradiated field after treatment of Hodgkin disease. The remainder of the patients were between 30 and 40 years old at diagnosis (Table 1). There were 61 men (64 percent) and 35 women (36 percent); the ratio of men to women was 1.74:1. Seven of our patients (7.2 percent) were black; there were no Mexican-Americans.

Smoking and Occupational History

Smoking histories were available for 88 of the 96 patients, and 90 percent of these 88 patients either smoked cigarettes or had done so at the time of diagnosis. Nine were nonsmokers and one patient smoked a pipe and cigars. There was essentially no difference in smoking habits between the men and women. Of the 61 men, 52 smoked (85 percent); of the 35 women, 27 smoked (77 percent). About 10 percent of both the men and women stated that they were nonsmokers; no smoking histories were available for the remaining few patients. Of the 78 patients who smoked cigarettes, the quantity of cigarettes smoked each day was available for 75. The median number of cigarettes smoked per day was 26, with a mean of 29. Ninety-five percent smoked 20 or more cigarettes a day and 32 percent smoked 40 or more a day. The length of time patients had smoked was available in 72 cases. The median/mean number of years was 18 (range 5 to 30 years). Only 10 percent had smoked for 12 years or less.

Occupational history was available for 88 patients; 5 of these gave a history of possible carcinogenic exposure. The five patients had the following occupations: silk-screen artist, micro-welder, sound technician (with exposure to asbestos), pipe fitter and beryllium miner. Most of the other patients had nonindustrial jobs and were housewives, sales people or office workers.

Symptoms, Weight Loss and Performance Status

Cough, chest pain, hemoptysis and fatigue were the most common presenting symptoms. In 12

LUNG CANCER IN YOUNGER PATIENTS

TABLE 2.—Stage at Diagnosis in 94 Patients

Stage of Disease	Percent
Resectable	20
Locally unresectable	40
Metastatic	40

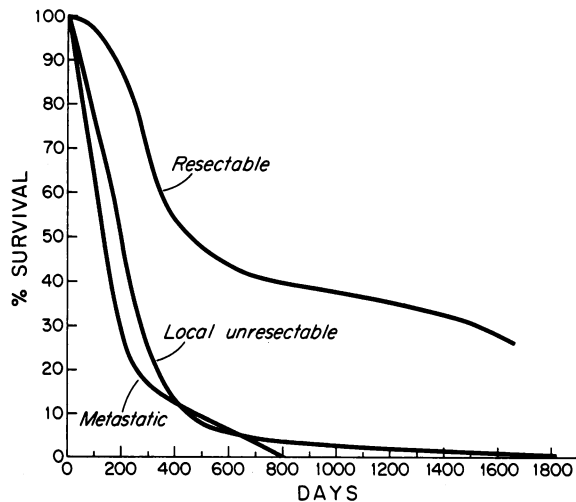


Figure 1.—Actuarial survival curves of patients according to stage of disease at presentation. The curves shown are smooth approximations to the Kaplan-Meier curves.

patients the diagnosis was made because of abnormal findings on an x-ray study of the chest. Information on weight loss was available in 52 cases and the median weight loss was 4.5 kg (10 pounds). The maximum was 33.8 kg (75 pounds) and 17 patients (32 percent) reported no weight loss. Karnofsky performance status could be assessed in only 42 cases. In these patients the median performance status was 78 percent.

Stage at Diagnosis and Treatment

Because this was a retrospective review, exact T,N,M staging (established by the International Union Against Cancer in the *UICC TNM Classification of Malignant Tumours*) could not be used. We have described each patient's stage at diagnosis as being resectable, locally unresectable or metastatic (Table 2). Pleural disease with positive cytologic findings was classified as metastatic, and positive hilar and mediastinal nodes were considered locally unresectable. Some 40 percent of the patients presented with metastasis to distant sites. Thirteen percent of all the patients presented with metastasis to the central nervous system, 5 percent to the liver and 21 percent to the bone.

Twenty percent of patients had operations intended to cure the disease (curative resection). Many others had operations in which only biopsies

were done when they were found to have unresectable tumors. Seventy-three percent of the patients received radiotherapy to either the primary tumor or areas of metastatic disease. Chemotherapy was given to 51 percent of the patients.

Pathological Findings

The distribution of the various histological cell types can be seen in Table 3. The relatively low incidence of squamous cell carcinoma is seen in the diagnosis as recorded in the chart, but more strikingly following review. Histological cell types are analyzed according to patients' sex in Tables 4 and 5. Among women there were slightly more cases of adenocarcinoma and fewer of small cell carcinoma. Adenocarcinoma of the lung has been thought to be unrelated to smoking¹⁰; however, of the 31 patients whose specimens were reviewed and found to have adenocarcinoma, 25 were smokers and 3 were nonsmokers; in 3 no information on smoking was available. Pathological diagnoses in nonsmokers included three cases of adenocarcinoma, one squamous, one undifferentiated and one unclassified.

Survival and Search for

Other Primary Sources of Malignancy

The median survival for the entire group of patients was about 27 weeks (190 days). To evaluate any improvements in the diagnosis and treatment of lung cancer which might have occurred during the 21 years of this review, survival was examined before and after January 1, 1966. There were 51 patients seen before January 1, 1966, and 45 patients after that time. For those treated from 1956 to 1965 the median survival was 26 weeks and for those treated from 1966 to 1976 it was 30 weeks ($P=0.55$, chi square=0.37 with 1 degree of freedom). When survival was assessed according to stage at presentation, there were 19 patients whose disease was considered resectable; their median survival was 69 weeks. The median length of survival for those with local unresectable disease was 28 weeks, and for those with metastatic disease it was 18 weeks (Figure 1). Survival curves were estimated using the method developed by Kaplan and Meier.¹¹ Comparisons between survival curves were made with the generalized Wilcoxon statistic developed by Breslow.¹² There was a statistically significant difference in survival for those patients whose disease was resectable compared with those in whom it was not ($P=0.001$, chi square=17.6, with 1 degree of freedom). There was no signifi-

cant difference in survival according to sex or pathological type; however, patients 35 years old or younger did better than those 36 to 40 years old (33 weeks survival versus 25 weeks median survival).

There were three long-term survivors (survival greater than five years free of disease) and one patient who died of other causes 14 years after the diagnosis of lung cancer. All four patients had curative resections; one had adjuvant radiation therapy and another required a subsequent resection for localized disease.

Another primary source of malignant disease was sought in 20 cases; this was done primarily in those patients with adenocarcinoma or undifferentiated carcinoma. No other source was found.

Data from the UCLA and California Tumor Registries

Between 1956 and 1976, there were 1,939 patients seen at UCLA with a diagnosis of lung cancer. Since 1968 there has been a steady increase in the number of lung cancer cases seen per year at UCLA, rising from 65 in 1968 to 142 in 1976, and reflecting the increasing incidence of lung cancer in the general population. However, the number of patients 40 years and younger with lung cancer has been relatively stable, ranging from four to six patients each year. Patients in this age range make up 5 percent of the UCLA Tumor Registry population. The median age of patients with lung cancer seen at UCLA was 58 years and the male to female ratio was 2.7:1.

The California Tumor Registry recorded 26,323 new cases of lung cancer between 1956 and 1976. Only 3 percent of the patients were 40 years old or younger. The median age of the population was 62 years and the male to female ratio was 3.0:1.

The median survival for all patients with lung cancer seen at UCLA was six months and in the California Tumor Registry population it was five months. Data from the UCLA and California tumor registries show that younger patients (aged 0 to 40 years) survived slightly longer, with median survival times of 6.3 months and 6 months, respectively.

Discussion

There are many similarities between the findings in our study population and others reported in the literature. In all of the reports that include both men and women there are more

women in the younger group than in the general population of patients with lung cancer. The ratio of men to women in these series^{4,5,7,8} varies from 3.25:1 to 2:1, in contrast to the general population of patients with lung cancer in which there is a greater proportion of males. Our findings of a male to female ratio of 1.74:1 is consistent with these other reports, while our general tumor registry population of patients with lung cancer had a ratio of 2.7:1. The relative increase in the number of women among the younger patients may reflect the more recent increase in smoking among women (1930 to 1949 versus 1900) and that the population of women at risk for lung cancer is, on the average, younger.¹³⁻¹⁵

Only a few of the series reporting on lung cancer in young patients included data on smoking history.^{2,5,6,8} In all of these studies 85 percent or more of the patients were smokers. Kyriakos and Webber⁶ reported that in their 27 patients younger than 40 the mean number of cigarettes smoked was 30 (1.5 packs) per day. Similarly, we found that of the 88 patients with available smoking history, 90 percent were cigarette smokers with a mean number of 29 cigarettes smoked per day. Thirty-two percent of those who smoked used 40 or more per day. The number of years our patients smoked (18 years) correlated with their age, as most patients began smoking in their late teen years.

There are some interesting findings regarding the histological type of lung cancer in younger patients. The American medical literature shows a preponderance of adenocarcinoma in these patients,^{2,4,6,7,9} with a range in relative incidence of this variety from 30 percent to 46 percent. The British literature⁵ suggests an increased incidence of oat cell carcinoma in young patients. This is in contrast to most series of patients of all ages where squamous cell carcinoma is the leading cell type.¹⁶⁻¹⁹ The converse of this observation is that squamous cell carcinoma occurs less frequently in young patients with lung cancer.

The pathological diagnosis recorded in the charts of our 96 patients shows an even distribution among adenocarcinoma, squamous cell carcinoma and undifferentiated carcinoma (Tables 3, 4 and 5). When 68 of the pathological specimens were reviewed using newer classification criteria, the high incidence of adenocarcinoma and paucity of cases of squamous cell carcinoma (irrespective of sex) in these young patients was even more striking. Because specimens were randomly obtained

LUNG CANCER IN YOUNGER PATIENTS

for review, we feel this is a fair representation of the true histological variation in this group.

Recent reviews of the histology of lung cancer suggest a general trend towards increased occurrence of adenocarcinoma.²⁰ This increased incidence in younger patients may be a reflection of this more general trend. This is of some importance because the survival of patients with non-squamous cell carcinoma is shorter in most series.^{21,22}

The major issue raised in the literature regarding lung cancer in younger patients is whether or not the disease is biologically more aggressive in this group. Younger patients would seem to have a higher potential for successful resections and cure because they lack serious underlying medical problems that might preclude operation. This same factor, however, may contribute to a delay

in seeking medical attention and further delay diagnosis until the disease is more advanced and no longer curable.

The rate of curative resections in young patients with lung cancer ranges from 18 percent in Neuman's series⁷ to 64 percent in the group of patients discussed by Kyriakos and Webber.⁶ The high rate of resection for cure in the latter series can be accounted for by the very aggressive approach taken by the surgeons at Barnes Hospital, St. Louis, as mentioned by the authors. Most series reviewed^{2,4,7-9} reported rates of curative resection of between 20 percent and 30 percent. Therefore, the findings of our study, in which 20 percent of the patients had operations with intention to cure, are comparable. The rate of curative resection in younger patients is similar to that in the general population of patients with lung cancer.²³

Most of the literature on younger patients with lung cancer discusses mean survival times; these range from 4.8 months in Putnam's series⁸ to 10.3 months in the series examined by Kyriakos and Webber.⁶ These survival rates seemed to be significantly influenced by the number of patients with squamous cell carcinoma in each series (reflecting a more favorable outcome), as well as the percentage of patients who had curative resections. The conclusions regarding survival in each series were directly related to these two factors. The median survival reported in our series was 6.3 months, and this reflects the modest rate of curative resection at our hospital as well as the relatively low incidence of squamous carcinomas in our patient population. After analysis of the survival data from our institution and from the California Tumor Registry, it would appear that the length of survival for younger patients with lung cancer is comparable to that of the general population of patients with lung cancer.

Conclusion

We have reviewed the clinical and pathological findings in 96 cases of bronchogenic cancer in patients 40 years old and younger seen at UCLA Hospital between 1956 and 1976. Our review is in agreement with the literature in finding a higher proportion of women among the younger patients with lung cancer, as well as a relatively low incidence of squamous cell carcinoma in this population. We have confirmed that lung cancer is largely a smoking-related neoplasm among

TABLE 3.—Distribution of Histological Cell Types

Histological Type	Diagnosis on Chart (96 Patients)		Diagnosis at Review (68 Patients)	
		Percent		Percent
Adenocarcinoma	27	28	31	46
Squamous	26	27	6	9
Small cell	6	6	11	16
Undifferentiated	24	25	16	24
Unclassified	10	10	3	4
Unknown	3	3
Insufficient data for diagnosis	1	1

TABLE 4.—Distribution of Histological Cell Types in Male Patients

Histological Type	Diagnosis on Chart (61 Patients)		Diagnosis at Review (37 Patients)	
		Percent		Percent
Adenocarcinoma	18	30	15	41
Squamous	16	26	2	5
Small cell	4	7	8	22
Undifferentiated	14	23	9	24
Unclassified	6	10	2	5
Unknown	3	4
Insufficient data for diagnosis	1	2

TABLE 5.—Distribution of Histological Cell Types in Female Patients

Histological Type	Diagnosis on Chart (35 Patients)		Diagnosis at Review (31 Patients)	
		Percent		Percent
Adenocarcinoma	9	26	16	52
Squamous	10	29	4	13
Small cell	2	5	3	10
Undifferentiated	10	29	7	22
Unclassified	4	11	1	3

LUNG CANCER IN YOUNGER PATIENTS

younger patients. We could find no significant improvement in length of survival among our patients that could be attributed to new therapeutic modalities (chemotherapy and radiotherapy), reflecting the fact that cure of this disease is related to surgical resection. In addition, by using comparative data from the UCLA and California tumor registries, we could find no significant difference in survival of younger patients compared with that of the general population of patients with lung cancer.

REFERENCES

1. Silverberg E: Cancer statistics, 1978. *C A* 28:17-32, 1978
2. Anderson AE, Buechner HA, Yager I, et al: Bronchogenic carcinoma in young men. *Am J Med* 16:404-415, 1954
3. Hanbury WJ: Bronchogenic carcinoma in young persons. *Br J Cancer* 12:202-206, 1958
4. Hood RH, Campbell DC, Dooley BN, et al: Bronchogenic carcinoma in young people. *Dis Chest* 48:469-470, 1965
5. Kennedy A: Lung cancer in young adults. *Br J Dis Chest* 66:147-154, 1972
6. Kyriakos M, Webber B: Cancer of the lung in young men. *J Thor Cardiovasc Surg* 67:634-648, 1974
7. Neuman HW, Ellis FH, McDonald JR: Bronchogenic carcinoma in persons under forty years of age. *N Engl J Med* 254:502-507, 1956
8. Putnam JS: Lung carcinoma in young adults. *JAMA* 238:35-36, 1977
9. Rivkin LM, Salyar JM: Bronchogenic carcinoma in men under 40 years of age. *Dis Chest* 34:521-524, 1958
10. Wynder EL, Berg JW: Cancer of the lung among non-smokers. *Cancer* 20:1161-1176, 1967
11. Kaplan EL, Meier P: Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 53:457-481, 1958
12. Breslow N: A generalized Kruskal-Wallis test for comparing K samples subject to unequal patterns of censorship. *Biometrika* 57:579-594, 1970
13. Wynder EL, Covey LS, Mabuchi K: Lung cancer in women: Present and future trends. *J Natl Cancer Inst* 51:391-401, 1973
14. Schneiderman MA, Levin DL: Trends in lung cancer. *Cancer* 30:1320-1325, 1972
15. Beamis JF, Stein A, Andrews JL: Changing epidemiology of lung cancer. *Med Clin North Am* 59:315-325, 1975
16. Kreyberg L: Lung tumors: Histology, aetiology and geographic pathology. *Union Internat Contra Cancrum* 15:78-95, 1969
17. Matthews MJ: Morphology of lung cancer. *Sem Onc* 1:175-182, 1974
18. Mountain CF: Surgical therapy in lung cancer: Biologic, physiologic and technical determinants. *Sem Onc* 1:253-258, 1974
19. Yesner R: Observer variability and reliability in lung cancer diagnosis. *Can Chem Rep, Part 3*, 4:55-57, 1973
20. Vincent RG, Pickren JW, Lane WW, et al: The changing histopathology of lung cancer. *Cancer* 39:1647-1655, 1977
21. Annegers JF, Carr DT, Woolner LB, et al: Incidence, trend and outcome of bronchogenic carcinoma in Olmstead County, Minnesota, 1935-1974. *Mayo Clin Proc* 53:432-436, 1978
22. Feinstein AR, Gelfman NA, Yesner R: The diverse effects of histopathology on manifestations and outcomes of lung cancer. *Chest* 66:225-229, 1974
23. Hyde L, Wolf J, McCracken S, Yesner R: Natural course of inoperable lung cancer. *Chest* 64:309-312, 1973